**Risk assessment, Preparedness, Prevention, and Response (PPR) framework for Yellow fever in Rwanda**

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**Abstract:**

**Background**

Yellow fever (YF) is a zoonotic arboviral disease that is mainly transmitted by *Aedes aegypti* and *Ae. albopictus* mosquitoes. It mainly infect both, human and non-human primates including the endangered mountain gorillas. Despite that Yellow fever is a vaccine preventable disease, according to the World Health Organization, it is still endemic in 47 countries; 72% of those countries are in Africa and 28% in Central and South America.

**Methodology**

### **We deployed several transdisciplinary research methods for the implementation of this risk assessment and situation analysis as well as developing national preparedness, prevention, and response strategy for YF in Rwanda. These methods included epidemiological and entomological surveys, health system analysis, and stakeholders and expert consultations. This was supported with in-depth desk and literature review analysis.**

**Results**

We have identified high risk of Yellow fever emergence and outbreaks in Rwanda. The main underpinning sources of this risk are including the confirmed presence of the main vector of the disease; *Aedes aegypti.* More importantly, the lack of vector surveillance for Aedes mosquitoes, surveillance for the disease among human or animals at risk in the country despite the ongoing transmission in the region including countries with open-borders and free movements with Rwanda. Additional important sources of risk include limited vaccination coverage and requirement for travelers to and from endemic countries. Accordingly, we have developed a preparedness, prevention, and response (PPR) framework for Yellow fever in Rwanda.

**Conclusion**

In addition to strengthen the implementation of the developed preparedness, prevention, and control measures, the One Health authority should invest in the establishment and operation of integrated surveillance and response system that comprehensively monitors the indicators of humans, animals, and environmental health. Additional support should be given to operational research to generate evidence that informs policymaking, and guide the strategic planning and implementation of cost-effective interventions.

**Keywords**: Pandemic preparedness, prevention, and response (PPPR) framework; Global Health Security; Arboviral diseases; Aedes-borne diseases; Africa

**Introduction:**

### **Yellow fever (YF) is a vaccine-preventable, mosquito-borne viral infection that has significantly impacted human health and socioeconomic stability and development for centuries** (1)**. As a member of the flavivirus family, the yellow fever virus (YFV) presents considerable public health challenges** (2)**. The historical trajectory of YF has influenced demographic shifts, public health policies, and economic structures, especially since the circulating strains of the virus first emerged in Africa over 1,500 years ago** (3)**. The disease predominantly affects individuals in Sub-Saharan Africa and tropical South America, with 40 countries categorized as endemic and at high risk for YFV outbreaks. Currently, YF continues to pose a threat, resulting in an estimated 109,000 cases and 51,000 deaths annually. These figures are likely underreported, as many YF cases remain undetected in many at-risk regions due to an inadequate laboratory diagnostic capacity, underdeveloped surveillance systems that are challenged with the disease’s nonspecific symptoms** (1,4)**.**

### **Recently, Africa including Rwanda is challenged by remarkable changes in climate, population growth and displacements, and globalization and unplanned urbanization. These factors collectively and interactively enhanced the emergence and development of emerging diseases outbreaks** (5,6)**.**

### **In Rwanda, zoonotic diseases including Rift Valley fever, mpox, Marburg virus, and other fungal infections are increasingly emerging** (7–12)**. Therefore, in response to these health emergencies, Rwanda Biomedical Center (RBC), the leading implementing agency for the health system in Rwanda, has initiated strategic plans and activities to strengthen the global health in the country and the region** (13)**. This includes conducting situation analysis and risk assessment exercises to identify diseases of high risk to Rwanda and develop a national preparedness, prevention, and response framework to strengthen the health system readiness to prepare, prevent, and response to these diseases outbreaks** (14)**. Therefore, here we report the risk assessment, preparedness, prevention, and response strategy of YF in Rwanda.**

### ****Methodology:****

### **We deployed several transdisciplinary research methods for the implementation of this risk assessment and situation analysis as well as developing national preparedness, prevention, and response strategy for YF in Rwanda. These methods included epidemiological and entomological surveys, health system analysis, and stakeholders and expert consultations. This was supported with in-depth desk and literature review analysis.**

### ****Transmission cycles host range**:**

### **The transmission of YFV occurs through a complex interplay of ecological factors within three primary transmission cycles: sylvatic, urban, and intermediate. In sylvatic environments, the virus is primarily spread by the bites of infected mosquitoes, particularly those from the *Aedes* and *Haemagogus* genera. Non-human primates serve as crucial reservoirs, becoming infected with the virus and facilitating its persistence in forested areas. When humans venture into these sylvatic zones, they can be exposed to infected mosquito bites, leading to sporadic outbreaks. In urban settings, the virus is transmitted between humans primarily through *Aedes aegypti* mosquitoes, which thrive in densely populated areas. This shift from sylvatic to urban transmission underscores the importance of mosquito control and surveillance in preventing outbreaks of YF in human populations (Fig. 1)** (15–18)**.**

### **C:\Users\TOSHIBA\Desktop\Yellow fever Rwanda\Figure Yellow fever cycle copy.tif**Figure 1.** Transmission cycles of Yellow fever in different ecological settings.**

### **The clinical presentation of YF typically begins with an incubation period of 3 to 6 days, during which the patient is asymptomatic. Initial symptoms may include fever, chills, loss of appetite, muscle aches, and other nonspecific signs that often resemble other locally endemic infections including malaria and other infections** (19–21)**. As the disease progresses, more severe symptoms may develop, such as abdominal pain, jaundice due to liver involvement, and gastrointestinal bleeding, often manifesting as black vomit. The fatality rate for YF ranges from 20% to 60%, with notably higher rates observed in children and individuals with underlying health conditions** (22)**.**

### **Despite the availability of safe and effective vaccines since the 1940s, YF outbreaks persist worldwide. Additionally, there is no specific antiviral treatment for YF infection; therefore, countries at risk should prioritize strengthening the implementation of the disease preparedness and prevention interventions including vaccination and effective vector control. This underscores the urgent need for increased investment in YF vaccination programs, particularly in endemic and high-risk countries** (2)**. The aim of the current report is to analyze the current situation regarding YF, assess preparedness, and provide strategic guidance on prevention and control measures in Rwanda.**

**Previous Risk Assessment of Yellow Fever in Rwanda**

**Rwanda, a landlocked country in East-Central Africa, has an estimated population of around 13 million people, characterized by a youthful demographic with a significant proportion under the age of 25** (10)**. Rwanda has made a substantial progress toward the control and elimination of endemic infectious diseases such as malaria, HIV/AIDS, tuberculosis** (19,23,24)**. However, due to climate change, globalization, and increased cross-borders dynamics of human and animals, the country is increasingly challenged by the emergence and spread of emerging zoonotic infectious diseases including arboviruses such as Rift Valley fever and other diseases** (7,25)**. Despite important advancements in healthcare and diseases management in Rwanda, still there is need for integrating the surveillance systems under the One Health strategy** (8)**. Additionally, the country is located in a region where YFV is endemic, and neighboring countries, including the Democratic Republic of the Congo (DRC) and Uganda, have reported YFV cases, raising concerns about potential cross-border transmission.**

A risk assessment exercise that was implemented in the country by local and international stakeholders of YF, mainly including Ministry of Health and WHO in 2014. This was complimented by another One Health prioritization exercise in 2024, that aimed to identify zoonotic diseases of public health importance in the country (14). Despite that the risk assessment exercise has suggested that the risk of the disease in the country is low. However, this was underestimation for the growing risk in the whole region including Rwanda as indicated by the recent ranking of YF as one of the top priority zoonotic diseases in the country (14). There are many other risk factors that were not counted for during the initial risk assessment exercise in 2014, also many risk factors have grown further over the last ten years. **Nevertheless, the assessment encompassed human, animal, and vector-related factors concerning YF. The findings revealed alarmingly low vaccine coverage, with only one out of 1,285 individuals surveyed having received the YF vaccine. Moreover, only 4.05% (n = 52) of the individuals tested positive for YF antibodies using ELISA, indicating low seroprevalence and highlighting a significant risk for YF in Rwanda** (26,27)**. Additionally, three participants demonstrated positive antibodies for other arboviruses, including dengue and Zika viruses, suggesting local transmission by the same mosquito vectors** (28,29)**.**

**The survey further investigated the presence of antibodies in non-human primates, specifically 16 Olive Baboons (*Papio anubis*) and 53 Vervet Monkeys (*Chlorocebus aethiops*). None of these animals tested positive for YF using plaque reduction neutralization test (PRNT) or serological methods, although seven were found to be positive for Zika virus IgG by ELISA** (30)**.**

**Regarding the vector composition in the country, various species were identified across Rwanda, including *Aedes spp*., *Anopheles spp.*, *Culex spp.*, *Mansonia spp.,* and *Coquilletidia spp*. All mosquito specimens were tested using RT-PCR, with results negative for the YF virus. Nevertheless, the presence of the main vector of YF; *Aedes aegypti* as well as minor vectors including *Ae. africanus* and *Ae. simpsoni* was confirm in the country** (30–33)**.**

**Unfortunately, the population survey for YF vaccination revealed a very low vaccination coverage with a single vaccinated person identified representing only 0.08% of the surveyed individuals. This low vaccination rate signals a heightened risk for potential YF outbreaks, especially in a region where the serosurvey detected antibodies suggesting prior natural exposure to the virus** (26,27,34)**.**

**Furthermore, of the 52 ELISA-positive samples tested, only 2 were confirmed as YFV positive through plaque reduction neutralization test (PRNT) analysis, resulting in a mere 0.16% of participants exhibiting naturally acquired antibodies. This data suggests that YFV may be circulating within the population, reinforcing the urgent necessity for enhanced surveillance and targeted vaccination campaigns to mitigate the risk of outbreaks.**

**Additionally, the non-human primate serosurvey indicated exposure to the Zika virus but found no evidence of exposure to YFV, West Nile virus (WNV), or Dengue virus (DENV). This lack of positivity could reflect either low prevalence of YFV among non-human primates or limited exposure to the virus, indicating the need for ongoing monitoring to understand transmission risks from these animal populations to humans. Moreover, the survey findings underscored the importance of monitoring endangered non-human primate populations, such as Olive Baboons and Vervet Monkeys, in understanding the dynamics of YFV transmission. As these species can serve as reservoirs for the virus, their conservation is crucial not only for ecological balance but also for reducing potential spillover events to human populations. As this survey was conducted in 2012, there has been no subsequent surveillance for YF in Rwanda, highlighting the need for updated assessments and enhanced preventive measures.**

**Yellow Fever Epidemiology in Africa (2014 – 2024):**

Over the past 10 year, the epidemiology of YF in Africa has undergone significant transformations, influenced by a combination of environmental changes, public health interventions, and evolving patterns in mosquito vector populations (35,36). As a mosquito-borne viral infection endemic to the continent, YF has historically imposed serious health risks on populations in endemic regions. Recent trends, notably the outbreak in Angola in 2015 - 2016 that spread extensively to the Democratic Republic of Congo, (DRC) with other countries such as China receiving infected travelers which were the first YF cases reported in China (37,38), have revealed both challenges and opportunities for effective disease management and control (39). In addition, two imported cases of YF in Kenya from Angola were reported and recorded in 2016 (40).

One concerning development has been the increase in reported YF cases in areas previously considered a low risk (41). Countries such as Nigeria and the DRC have faced localized outbreaks, even amidst ongoing vaccination campaigns. This resurgence can largely be attributed to rising mosquito vector populations and environmental conditions conducive to mosquito breeding, including wetter weather patterns linked to climate change (39,41). The presence of competent mosquito vectors, such as *Aedes aegypti* and other *Haemagogus* species, is critical for the YF virus's transmission cycle. The growth of these vector populations has heightened the risk of outbreaks in vulnerable urban and peri-urban areas (42). Furthermore, population mobility enhances the risk of new virus introductions and outbreaks, particularly in urban centers and non-endemic regions populated by competent vectors like *Aedes aegypti*. The global threat is exacerbated by the potential for similar mosquito-borne viruses, such as chikungunya, dengue, and Zika, to spread into regions currently free of YF, highlighting the need for sustained vigilance and robust public health strategies to combat this persistent public health challenge (36).

The impact of vaccination campaigns varies significantly across regions. While countries like Ghana and Senegal have successfully boosted vaccination coverage through comprehensive mass immunization initiatives, considerable gaps continue to exist, particularly in conflict-affected or remote regions (1). The International Federation of Red Cross and Red Crescent Societies (IFRC) and the World Health Organization (WHO) are actively promoting the importance of covering all at-risk populations with vaccination.

**Recent Yellow fever outbreaks in the region**:

Despite these significant achievements, YF outbreaks persist. Even as vaccination coverage has improved, rising from 20 million doses produced annually two decades ago to over 150 million doses in recent years. The COVID-19 pandemic and other health emergency events such as Ebola outbreaks in West Africa, have severely disrupted the delivery of healthcare and public health services including the routine immunization programs, with coverage in some countries decreasing from 72% in 2010 to 65% by 2020. As a result, nine countries reported average YF immunization coverage below 60% (43). Unfortunately, this might have contributed to the growing outbreaks of YF throughout the African region (Fig. 2). This is highlighted by about four outbreaks reported through east, central, and west Africa regions.

**C:\Users\ahmeay\Documents\Projects\Collaborations\Rwanda\DG\High dangerous pathogens\Yellow fever\Africa map diseases-01.tifFigure 2.** Map of Africa shows the distributions of Yellow fever outbreaks including number of cases and deaths reported over the last decade between 2015 and 2024. Rwanda highlighted in black.

**Risk of Yellow fever in Rwanda:**

Rwanda is located in middle of a hotspot of YF outbreaks, this is indicated by that all the neighboring countries except Burundi have reported cases and/or deaths of YF (Fig. 2). Additionally, the risk assessment that was implemented in the country in 2014, has confirmed the presence of the main competent vector of YF; *Aedes aegypti*, in the country. Unfortunately, in lack of routine vectors surveillance system that monitor local population of *Ae. aegypti* and its involvement in diseases transmission in the country, this risk is left growing uncontrollably. Accordingly, this is limiting the capacity to implement cost-effective vector control interventions targeting the primary vectors of YF. Additionally, lack of such surveillance system increase the country vulnerability to the risk of the emergence of invasive diseases vectors such as *Ae. albopictus* in the country, which is increasing growing in the region leading to remarkable changes in arboviral diseases epidemiology (33,42,44,45). Particularly that environmental suitability and communities connectivity model showed that Rwanda is at high risk of Ae. Albopictus emergence and local establishment (45).

Furthermore, Rwanda has a policy cross-borders open movement for African people from throughout the world with limited implementation of enforcing the requirement for YF vaccination at entry for international travelers. This expose the country to high risk with thousands of people moving daily in and out of the country. According to the World Health Organization (WHO), YF is endemic in 34 countries in Africa and 13 countries in Central and South America (46). This underscores substantial risk of introducing YF in the country, particularly that evidence shows that the closely related virus of dengue fever was introduced in some areas through travelers between endemic and disease-free areas (47–49). Moreover, the lack of routine surveillance for YF among human and the animal hosts including the endangered species of mountain gorilla, keeps human and animal health systems blind from the potentially growing risk of the disease in the country. This highly potential is highlighted by the WHO recommendation for travelers from Rwanda older than one year to be vaccinated for YF (50). This strategy will mainly prevent Rwandan travelers from exporting the disease from Rwanda to other countries or imported back into their country upon return.

**Preparedness for Yellow Fever Risk in Rwanda**

Yellow fever presents a significant health threat in many regions, particularly in parts of Africa, including Rwanda, and South America. To combat this preventable disease, establishing a comprehensive framework for preparedness and response is essential.

Effectively mitigating the risk of YF in Rwanda necessitates the development of a robust preparedness framework (Fig. 3). This framework should include a comprehensive surveillance system to monitor YFV activity and mosquito populations, as well as the strategic allocation of public health resources to identified high-risk areas.

**C:\Users\ahmeay\Documents\Projects\Collaborations\Rwanda\DG\Special pathogens\Yellow fever\Figure 2.tif Figure 3**. Core pillars of an integrated One Health preparedness, prevention, and response strategy for Yellow fever in Rwanda.

Preparedness involves not only developing a comprehensive surveillance system to monitor YFV activity and mosquito populations but also ensuring that public health resources are strategically allocated to areas identified as high risk.

The first line of defense against YF is the establishment of an Early Warning, Alert, and Response System (EWARS). This system is critical for timely identification and response to potential outbreaks. Stakeholders in the health care sector must continuously monitor data to ensure that alerts are generated as soon as there are signals indicating a potential outbreak, allowing for swift action to protect communities.

To this end, health authorities should prioritize the enhancement of vaccination campaigns targeting vulnerable populations in proximity to identified ecological zones that exhibit favorable conditions for YFV transmission. Investing in vaccination and improving vaccine coverage for YF in Rwanda is critical for strengthening the country's preparedness against potential outbreaks. A comprehensive vaccination strategy should emphasize not only the development and distribution of effective vaccines but also ensuring accessibility for all communities, particularly those in remote and high-risk areas. Public health campaigns must be designed to effectively inform the population about the benefits of vaccination, combating vaccine hesitancy through education and outreach. Collaboration with local health organizations can facilitate mobile vaccination units to reach underserved populations, ensuring that no community is left vulnerable. By increasing vaccine coverage through targeted initiatives and mobilizing resources, Rwanda can build herd immunity, significantly reducing the likelihood of YF transmission and fostering greater public health security for its citizens. Additionally, investing in both vaccine research and infrastructure will be pivotal in the ongoing battle against YF and other mosquito-borne diseases, paving the way for a healthier future.

Community engagement will be a vital component of preparedness efforts. Public health education initiatives should focus on increasing awareness about YF transmission, symptoms, and the importance of vaccination. Training community health workers to identify potential outbreak scenarios and report them to health officials can help create an early alert and response system that is both proactive and reactive to emerging threats (51). Furthermore, integrating vaccination campaigns with other public health interventions, can streamline the decisionmaking, strategic planning, and implementation of interventions for multiple public health concerns simultaneously (52).

A multi-sectoral approach involving environmental management is essential for effective preparedness. Conserving endangered primate species like the Olive Baboon is critical as their habitats overlap with areas where YFV circulates. Coordinated efforts between health authorities and environmental agencies can facilitate habitat assessments, ensuring that conservation strategies align with mosquito control efforts to mitigate transmission risks. Given Rwanda's diverse landscapes, public health responses must tailor vector control measures to specific ecological conditions, adopting localized strategies that consider both urban and rural settings.

Moreover, building capacity in local health systems and laboratories is equally important for effective preparedness. Establishing well-equipped laboratories capable of testing for YFV and other mosquito-borne diseases will improve diagnostic capabilities and facilitate timely responses to suspected outbreaks. Training healthcare personnel in laboratory protocols, surveillance techniques, and data analysis is essential for creating a knowledgeable workforce that can respond swiftly and effectively. This capacity-building initiative should also include enhancing the skills of laboratory technicians and integrating modern technologies for disease detection and monitoring.

Finally, fostering partnerships with regional and international health organizations will contribute to enhanced preparedness by facilitating knowledge exchange, resource sharing, and research collaborations. Establishing a collaborative platform can support continuous monitoring of disease patterns and capacity-building initiatives to equip health workers with the skills needed to manage potential YF outbreaks. By cultivating a culture of preparedness—focusing on vaccination, community engagement, laboratory capacity, and environmental management—Rwanda can better safeguard its population against the looming threats posed by YF, ensuring both community resilience and public health security.

**Conclusion and way forward:**

The major outcome of these risk assessment, situation analysis, and One Health zoonotic diseases prioritization exercises and continuation of RBC’s policy of leading evidence-based improvement of healthcare and public health services in the country, it has initiated the process to ensure that people at risk of YF are vaccinated as well as enforcing the requirement of YF vaccination for national and international travelers.

The evident threat of YF in Rwanda underscores the urgent need for comprehensive up to date risk assessment, robust epidemiological and entomological surveillance systems, cost-effective preparedness, prevention, and control measures. With a historical backdrop of low vaccination coverage and limited surveillance, the potential for YF outbreaks remains significant, particularly given the country’s geographical proximity to endemic regions and countries where YFV transmission has occurred. The previous risk assessment highlighted alarming gaps in vaccination, seroprevalence, and vector monitoring, culminating in an imperative call for enhanced public health interventions.

As Rwanda moves forward, establishing a robust preparedness framework that encompasses a multi-faceted approach is essential. Strengthening surveillance systems, launching targeted vaccination campaigns, and fostering community engagement are foundational components needed to mitigate the risk of YF. Furthermore, integrating efforts aimed at controlling other mosquito-borne diseases will optimize public health resources and enhance the overall effectiveness of interventions.

A "One Health" approach is particularly vital, recognizing the interconnectedness of human, animal, and environmental health. By engaging multiple sectors—including health, wildlife management, and environmental agencies—Rwanda can effectively address the complex ecological factors contributing to YF transmission. Collaborative efforts will facilitate comprehensive habitat assessments, integrated pest management strategies, and continuous monitoring, ultimately fostering resilience against the threats posed by YF and other infectious diseases.

In conclusion, through proactive risk management, community involvement, and a One Health perspective, Rwanda can better prepare for, prevent, and respond to YF outbreaks if they ever occurred in the country. This will ensure the safety, health, wellbeing, and socioeconomic stability and growth of the country population while promoting public health security in the region.

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